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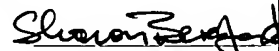
April 15, 2004

## CERTIFICATE OF MAILING 37 C.F.R 1.8

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April 15, 2004

Date

  
Sharon A. Beresford

**MS DD**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

RE: *U.S. Patent Application No. 10/767,217 entitled "METHODS AND COMPOSITIONS FOR ANALYSIS OF MITOCHONDRIAL-RELATED GENE EXPRESSION" – John Papaconstantinou et al.*  
*Our reference: CLFR:021US*

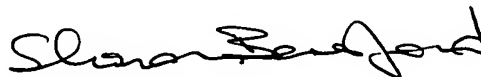
Sir:

Enclosed for filing in the above-referenced patent application is an Information Disclosure Statement, Form PTO-1449, and references C1-C33.

No fees are believed to be due in connection with the filing of this Information Disclosure Statement, however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be deemed necessary for any reason relating to the enclosed materials, the Commissioner is authorized to deduct the appropriate fees from Fulbright & Jaworski Deposit Account No.: 50-1212/CLFR:021US.

Please date, stamp and return the enclosed postcard evidencing receipt of these materials.

Respectfully submitted,



Sharon A. Beresford  
Reg. No. 52,615  
Patent Agent

SAB/kmv  
Encl.: as noted



**PATENT**

In re Application of:

John Papaconstantinou *et al.*

Serial No.: 10/767,217

Filed: January 29, 2004

For: METHODS AND COMPOSITIONS FOR  
ANALYSIS OF MITOCHONDRIAL-  
RELATED GENE EXPRESSION

Group Art Unit: Unknown

Examiner: Unknown

Atty. Dkt. No.: CLFR:021US

**CERTIFICATE OF MAILING**  
37 C.F.R. 1.8

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April 15, 2004

Date

  
Sharon A. Beresford

**INFORMATION DISCLOSURE STATEMENT**

**MS DD**

Commissioner for Patents

P.O. Box 1450

Alexandria, Virginia 22313-1450

Sir:

In compliance with the duty of disclosure under 37 C.F.R. § 1.56, it is respectfully requested that this Information Disclosure Statement be entered and the documents listed on attached Form PTO-1449 be considered by the Examiner and made of record. Copies of the listed documents required by 37 C.F.R. § 1.98(a)(2) are enclosed for the convenience of the Examiner.

In accordance with 37 C.F.R §§ 1.97(g), (h), this Information Disclosure Statement is not to be construed as a representation that a search has been made, and is not to be construed to be

an admission that the information cited is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

The present Information Disclosure Statement is being filed prior to the receipt of a first Official Action reflecting an examination on the merits, and hence is believed to be timely filed in accordance with 37 C.F.R. § 1.97(b). No fees are believed to be due in connection with the filing of this Information Disclosure Statement, however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be deemed necessary for any reason relating to these materials, the Commissioner is authorized to deduct the appropriate fees from Fulbright & Jaworski Deposit Account No.: 50-1212/CLFR:021US.

Applicants respectfully request that the listed documents be made of record in the present case.

Respectfully submitted,



Sharon A. Beresford  
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Agent for Applicants

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Date: April 15, 2004

Form PTO-1449 (modified)

Atty. Docket No.

CLFR:021US

Serial No.

10/767,217

List of Patents and Publications for Applicant's

Applicant

John Papaconstantinou *et al.*

INFORMATION DISCLOSURE STATEMENT

Filing Date:

January 29, 2004

Group:

Unknown

(Use several sheets if necessary)

U.S. Patent Documents

See Page 1

Foreign Patent Documents

See Page 1

Other Art

See Page 1

## U.S. Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Name	Class	Sub Class	Filing Date of App.

## Foreign Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Country	Class	Sub Class	Translation Yes/No

## Other Art (Including Author, Title, Date Pertinent Pages, Etc.)

Exam. Init.	Ref. Des.	Citation
	C1	Ames <i>et al.</i> , "Oxidants, antioxidants, and the degenerative diseases of aging," <i>Proc. Natl. Acad. Sci., USA</i> , 90:7915-7922, 1993.
	C2	Anderson <i>et al.</i> , "Sequence and organization of the human mitochondrial genome," <i>Nature</i> , 290:457-465, 1981.
	C3	Ballinger <i>et al.</i> , "Hydrogen peroxide- and peroxynitrite-induced mitochondrial DNA damage and dysfunction in vascular endothelial and smooth muscle cells," <i>Cir. Res.</i> , 86:960-966, 2000.
	C4	Beckman and Ames, "The free radical theory of aging matures," <i>Physiol. Rev.</i> , 78:547-581, 1998.
	C5	Beckman and Ames, "Endogenous oxidative damage of mtDNA," <i>Mutat. Res.</i> , 424:51-58, 1999.
	C6	Corral-Debrinski <i>et al.</i> , "Hypoxemia is associated with mitochondrial DNA damage and gene induction," <i>JAMA</i> , 266(13):1812-1816, 1991.
	C7	Corral-Debrinski <i>et al.</i> , "Association of mitochondrial DNA damage with aging and coronary atherosclerotic heart disease," <i>Mutat. Res.</i> , 275:169-180, 1992.
	C8	Corral-Debrinski <i>et al.</i> , "Mitochondrial DNA deletions in human brain: regional variability and increase with advanced age," <i>Nat. Genet.</i> , 2:324-329, 1992.
	C9	Corral-Debrinski <i>et al.</i> , "Marked changes in mitochondrial DNA deletion levels in Alzheimer brains," <i>Genomics</i> , 23:471-476, 1994.

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INFORMATION DISCLOSURE STATEMENT — PTO-1449 (MODIFIED)

Form PTO-1449 (modified)		Atty. Docket No. CLFR:021US	Serial No. 10/767,217
List of Patents and Publications for Applicant's  INFORMATION DISCLOSURE STATEMENT  (Use several sheets if necessary)		Applicant John Papaconstantinou <i>et al.</i>	
		Filing Date: January 29, 2004	Group: Unknown
U.S. Patent Documents <i>See Page 1</i>	Foreign Patent Documents <i>See Page 1</i>	Other Art <i>See Page 1</i>	

### Other Art (Including Author, Title, Date Pertinent Pages, Etc.)

Exam. Init.	Ref. Des.	Citation
	C10	Finkel and Holbrook, "Oxidants, oxidative stress and the biology of ageing," <i>Nature</i> , 408:239-247, 2000.
	C11	Golden and Melov, Mitochondrial DNA mutations, oxidative stress, and aging," <i>Mech. Aging Dev.</i> , 122:1577-1589, 2001.
	C12	Harmon, <i>Am. "The biological clock: the mitochondria?" J. Geriatric Soc.</i> , 20(4):145-147, 1972.
	C13	Horton <i>et al.</i> , "Marked increase in mitochondrial DNA deletion levels in the cerebral cortex of Huntington's disease patients," <i>Neurology</i> , 45(10):1879-1888, 1995.
	C14	Hsieh <i>et al.</i> , "The effect of aging on p38 signaling pathway activity in the mouse liver and in response to ROS generated by 3-nitropropionic acid," <i>Mech. Aging Dev.</i> , 123:1423-1435, 2002.
	C15	Jun <i>et al.</i> , "A mitochondrial DNA mutation at nucleotide pair 14459 of the NADH dehydrogenase subunit 6 gene associated with maternally inherited Leber hereditary optic neuropathy and dystonia," <i>Proc. Natl. Acad. Sci., USA</i> , 91:6206-6210, 1994.
	C16	Jun <i>et al.</i> , "Use of transmitochondrial cybrids to assign a complex I defect to the mitochondrial DNA-encoded NADH dehydrogenase subunit 6 gene mutation at nucleotide pair 14459 that causes Leber hereditary optic neuropathy and dystonia," <i>Mol. Cell. Biol.</i> , 16(3):771-777, 1996.
	C17	Mandavilli <i>et al.</i> , "Mitochondrial DNA repair and aging," <i>Mutation Res.</i> , 509:127-151, 2002.
	C18	Melov <i>et al.</i> , "Marked increase in the number and variety of mitochondrial DNA rearrangements in aging human skeletal muscle," <i>Nucleic Acids Research</i> , 23(20):4122-4126, 1995.
	C19	Melov <i>et al.</i> , "Multi-organ characterization of mitochondrial genomic rearrangements in ad libitum and caloric restricted mice show striking somatic mitochondrial DNA rearrangements with age," <i>Nucleic Acids Research</i> , 25(5):974-982, 1997.
	C20	Melov <i>et al.</i> , "Extension of life-span with superoxide dismutase/catalase mimetics," <i>Science</i> , 289:1567-1569, 2000.
	C21	Mitochondria and Free Radicals, In: <i>Neurodegenerative Diseases</i> , Beal <i>et al.</i> (ed.), Wiley-Liss, NY, 1997.
	C22	Papaconstantinou, "Unifying model of the programmed (intrinsic) and stochastic (extrinsic) theories of aging," <i>Annals of the New York Academy of Sciences</i> , 719:195-211, 1994.

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Form PTO-1449 (modified)		Atty. Docket No. CLFR:021US	Serial No. 10/767,217
List of Patents and Publications for Applicant's  INFORMATION DISCLOSURE STATEMENT  (Use several sheets if necessary)		Applicant John Papaconstantinou <i>et al.</i>	
		Filing Date: January 29, 2004	Group: Unknown
U.S. Patent Documents <i>See Page 1</i>	Foreign Patent Documents <i>See Page 1</i>	Other Art <i>See Page 1</i>	

### Other Art (Including Author, Title, Date Pertinent Pages, Etc.)

Exam. Init.	Ref. Des.	Citation
	C23	Saito and Papaconstantinou, "Age-associated differences in cardiovascular inflammatory gene induction during endotoxic stress," <i>J. Biol. Chem.</i> , 276(31):29307-29312, 2001.
	C24	Santos <i>et al.</i> , "Measuring oxidative mtDNA damage and repair using quantitative PCR," <i>Methods Mol. Biol.</i> , 197:159-176, 2002.
	C25	Shoffner <i>et al.</i> , "Spontaneous Kearns-Sayre/chronic external ophthalmoplegia plus syndrome associated with a mitochondrial DNA deletion: a slip-replication model and metabolic therapy," <i>Proc. Natl. Acad. Sci., USA</i> , 86:7952-7956, 1989.
	C26	Shoffner <i>et al.</i> , "Myoclonic epilepsy and ragged-red fiber disease (MERRF) is associated with a mitochondrial DNA tRNA <sup>Lys</sup> mutation," <i>Cell</i> , 61:931-937, 1990.
	C27	Shoffner <i>et al.</i> , "Mitochondrial DNA variants observed in Alzheimer disease and Parkinson disease patients," <i>Genomics</i> , 17:171-184, 1993.
	C28	Ventura <i>et al.</i> , "Control of oxidative phosphorylation by Complex I in rat liver mitochondria: implications for aging," <i>Biochim. Biophys. Acta</i> , 1553:249-260, 2002.
	C29	Wallace <i>et al.</i> , "Familial mitochondrial encephalomyopathy (MERRF): genetic, pathological, and biochemical characterization of a mitochondrial DNA disease," <i>Cell</i> , 55:601-610, 1988.
	C30	Wallace, "Mitochondrial diseases in man and mouse," <i>Science</i> , 283:1482-1488, , 1999.
	C31	Waterson <i>et al.</i> , "A sociotechnical method for designing work systems," <i>Human Factors</i> , 44(3):376-391, 2002.
	C32	Waterston <i>et al.</i> , "Initial sequencing and comparative analysis of the mouse genome," <i>Nature</i> , 420:520-562, 2002.
	C33	Zhang <i>et al.</i> , "Multiple mitochondrial DNA deletions in an elderly human individual," <i>FEBS Lett.</i> , 297:34-38, 1992.

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